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10/712,423	11/13/2003	Hamdi K. Hamdi	HAMDI-001B	9959

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,423	HAMDI ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/9/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-14,16-31,33 and 37-71* is/are pending in the application.

4a) Of the above claim(s) *12-14,16 and 37-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-11,17-31 and 33* is/are rejected.

7)☒ Claim(s) *3 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/14/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed 3/9/07 presents remarks and arguments to the office action mailed 6/20/06. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on is acknowledged and has been reviewed.

The information disclosure statement filed see last two documents fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because they are not a published document. It has been placed in the application file, but the information referred to therein has not been considered as to the merits.

Status of claims

Claims 1, 3, 5 -11, 15 and 17-31 and 37-71 are pending.

Claims 37-71 remain withdrawn from examining as to a non elected species.

Claims 1, 3, 5-11, 15, and 17-31 and 33 are examined in this office action.

Claim Objections

Claims 3 and 11 are objected for having multiple periods in the claim. A claim should only contain one period. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 7-8, 9-11, 17-23, 24-30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meisner, US 6,440,465 in view of Cuomo et al., US 6,358,542 taken with Crea et al., 20030108651.

Meisner, teaches administering oleuropein (see col. 4, lines 42) for the treatment of skin condition-psoriasis. From the teaching skin cancer is taught as one of the skin

conditions (see col. 3, lines 20-65). Therefore one of ordinary skill in the art would have been motivated to use oleuropein for the treatment of melanoma cancer as required by claims 1, 3, 7, 8, 11, 24 and 30. The properties such as anti-growth, anti-motality or anti-metastasis are part of the compound, therefore as stated in the MPEP 2112.01"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Meisner also teaches the compound can be topically applied (see col. col. 10 studies 2-4, where the formulation is a cream.

Cuomo et al., teach administering oleuropein (see col. 2, lines 15-25) for the treatment of cancer as required by instant claims 26-28. As stated above the properties of the compound as to inhibiting the growth, motility invasiveness and metastasis will be obvious because the compound is the same.

Crea et al., teach the different forms of administering oleuropein as parenterally orally, intramuscularly and intravenously see para. 0087.

One of ordinary skill in the art would have been motivated to administer the same compound oleuropein to patients with cancer for instant treating cancer of the skin. The Meisner reference teach treating skin conditions that develop into skin cancer with the claimed compound. . It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the compound oleuropein, as suggested by Meisner, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because The motivation comes from Meisner that the compounds are used to treat cancer especially skin cancer A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

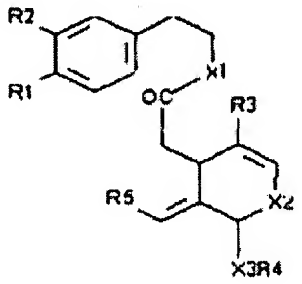
Maintained Claim Rejections - 35 USC § 112-first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant amending the claims did not overcome the below rejection, therefore the rejection is maintained. Because, there is no argument to the below rejection, Examiner have repeated the rejection.

I. Claims 26-28, 30-31 and 33remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting colon cancer cell migration *in vitro* and *in vitro* modulation of unregulated cell growth does not reasonably provide enablement for treating a wide variation of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims refer to "treating a medical condition" having chemopreventive activity with the



compound , based upon that, the applicant has not shown any invivo result to convey this. In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, 7) the relative skill of those skilled in the art and 8) the quantity of experimentation needed.

Response

Although, Applicant has in part addressed a section of the enablement rejection raised, the question still remain with regards to how one compound is capable of

treating a very wide variation of cancer cells. Considering that every medication in other for it to kill the cells must contact the cell wall, this is not new in the art of cancer and treatment. In the art of cancer treatment, there is no one drug that is capable of treating cancer, especially, emphasis added a wide variation of cancers.

The affidavit submitted has been carefully, however, Applicant has still not shown with data how the skilled artisan would be able to practice treating various types of cancers with this drug successfully. Merely, stating that the drug is capable of treating because it acts on the cell wall is insufficient and does not give the monopoly asserted by the claim.

Applicant's arguments filed have been fully considered but they are not persuasive. For the reasons stated above. The rejection is hereby maintained and repeated.

Rejection (based on the composition to treat any type of cancer)

1) Nature of the invention.

The nature of the invention is a method for treating a cancer in a subject comprises administering the instant pharmaceutical composition to a patient (mammal) in need thereof. As stated, however, claims 1, 5, 10, 20, 24, 29, 31 and 35 recite that any cancer is intended or a very wide variation of cancer.

2) State of the prior art and the predictability or lack thereof in the art.

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibited the desired pharmacological activities (i.e. what

compounds can treat which specific disease eg., colon, breast, lung etc). The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between the claimed compound as capable of treating medical condition which involves inhibiting colon cancer cell migration, modulation of unregulated cell growth in vivo as well as in vitro, one of skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of the claimed compound in vivo. Emphasis again added Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para).

Also, more recently with regards to unpredictability, Johnson et al (British J. of Cancer 2001, 84(10) 1424-1431) teaches the use of 39 agents invivo activity in a

particular histology in a tumor model did not closely relate to activity in the same human cancer. Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed compound composition could be predictably used as an anti-cancer agent for any type of medical conditions which involves cancer as inferred by the claim and as contemplated by the specification. Further, the refractory nature of cancer to drugs is well known in the art

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would first need to determine the type of cancer to be treated, and then determine what dosage of the claimed compounds would be suitable for said treatment and/or prevention without toxicity to the patient in need thereof. Guru et al taken with Johnson et al (cited above makes it clear that much more than routine experimentation is needed).

4) Level of predictability in the art.

The art pertaining to the treatment of a/any medical condition which involves cancer remain highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art. Firstly, the mode of action in vitro is different from the mode of action invivo. Even within the animal models, a compound effective against cancer or a disease associated with cancer with a positive result in an animal model does not necessarily mean a positive result in humans. Cancer is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical

pathways that mediate the cancer reaction. There is no common mechanism by which any, or even most, cancer arise.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is no where found in the specification. However, the gap between *in vitro* activity and *in vivo* utility is large enough to warrant thorough and compelling *in vivo* or clinical data.

6) Existence of working examples.

As discussed above, no working example is found in the current application. Applicant's omission of working examples does not enable one of ordinary skill in the art to treat all cancers encompassed by the instant invention.

7) Breadth of claims.

The claims are extremely broad due to the recitation of all a wide variety and forms of cancer encompassed by the instant invention.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of any disease. As a result necessitating one of ordinary skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

II. **Rejection based on treating any type of cancer with one compound.**

1) The nature of the invention: The nature of the invention is treating all medical conditions associated with cancers which is extremely broad. For example pancreatic cancer, there is hardly a cure for this type of cancer. In view of the report Pancreatic cancer 2006, 90% of patients die within 12 months of diagnosis.

2) The state of the prior art: There are no examples shown in the specification on how to treat any cancer using the compound invivo. The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which cancer cell was inhibited by the compound. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting an invitro regime on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between treating conditions of any-type of cancer, one of skill in the art is unable to fully predict possible results from the administration of the compound due to the unpredictability of the role of the diseases.

3) The predictability or lack thereof in the art: there is currently no completely effective therapy for treating a genus medical condition which are cancer, with one compound. Search for therapeutic agents useful for the treatment of cancer is ongoing. For example: The art pertaining to the treatment of cancer of any type of cancer remain highly unpredictable because there is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the disease.

4) The amount of direction or guidance present -The specification only provides examples to treating colon cell (invitro) and wounds (invitro). While the invitro examples may suffice as a preliminary step into the research, it no-where shows how one can extrapolate the date to an invivo testing. The examples shown will not enable one skilled in the art to treat any types of cancerous diseases.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present found on pages 20-26 is not sufficient to enable one of skill in the art to treat all medical conditions that are cancers in vivo which embraces a myriad of conditions

6) Existence of working examples.

As discussed above, the working examples are found on pages 20-26 are insufficient for such a broad claim of treatment of all disease of angiogenesis. Applicant's limited working example does not enable one of ordinary skill in the art to treat all medical conditions which are cancer in the instant invention.

7) Breadth of claims.

Claim 1 is extremely broad due to the recitation of all types and forms of cancer encompassed by the instant invention.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which cancers exhibit inhibitory effect of the instantly claimed compound.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of all cancers. As a result necessitating one of skill in the art to perform an exhaustive search to determine which diseases can be treated by the compound(s) of the instant claims in order to practice the claimed invention.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms, and treatment (or lack thereof) for cancer.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
10/6/07

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